



State of the U.S. Drug Regulatory System

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- Purpose of this meeting:
 - Input from stakeholders
- Purpose of this talk:
 - Scope of drug regulatory activities
 - Sense of current priorities and issues



Agenda

- Current drug regulatory system & public expectations
- Scope of activities and resources available
- Current level of performance & issues
- Summary

Topics

U.S. Drug Regulatory System

- In evolution over much of the 20th Century
- **Mission:** Promote and protect public health by assuring that safe and effective drugs are available to Americans.
- **Most recent modification:** FDA Modernization Act of 1997

Components of System

- **FDA**
 - Center for Drug Evaluation and Research
 - Office of Regulatory Affairs (FDA Field)
 - Office of Chief Counsel
 - Office of the Commissioner

Components of System (cont.)

- State and Local Officials
 - State Licensing Boards
- Institutional Review Boards
- DEA

Expectations for the System

- **All marketed drugs are effective and safe in the context of their use.**
 - Human drugs are of high quality
 - Generic competition keeps drug prices reasonable
 - All advertising and promotion of drugs is informative and is not false or misleading

Expectations for the System (cont.)

- **Patients who lack alternatives have access to investigational drugs**
- **High quality information on how to use drugs is available including information on children, elderly patients and other groups**

Expectations for the System (cont.)

- **Robust drug development programs, that thoroughly protect human subjects, flourish and are productive**

Drug Regulatory System: Processes

- ⊗ **Application Review**
 - IND, New Drug Application
 - ANDA
- ⊗ **Standard Setting**
 - OTC Monographs
 - Standards for Marketing
 - Technical Standards
 - Quality Standards
 - Format and Content

Drug Regulatory System: Processes (cont.)

- ⊗ **Post-marketing safety surveillance (Pharmacovigilance)**
 - Post-marketing trials, registries
 - Spontaneous reporting system
- ⊗


Drug Regulatory System: Processes

- ⊗ **Compliance /Enforcement**
 - Inspections
 - Surveillance
 - Drug sampling
 - Advertising
 - Education
 - Regulatory Actions




Drug Regulatory System: Essential Supporting Activities

- Research
 - Laboratory
 - Regulatory Science
 - Policy Development
- Policy Development
- International Collaboration/Outreach



Essential Supporting Activities

- Communication
 - Drug information/education
 - Freedom of information process
 - Dispute resolution
 - CDER Ombudsman
 - Citizen Petition process
 - Stakeholder feedback - ORA



Essential Supporting Activities:

- Information Management
 - Information technology
 - Medical library
 - Electronic submissions
 - Intra- and Internet - use

Essential Supporting Activities:

- Training
 - Internal
 - Policies
 - Procedures
 - External


FDA Drug Regulatory Program: 1998 Resources*

- 2,561 People
1,708 CDER
853 ORA (field)
- \$283,953.00 Budget
206K CDER
11.5K Orphan Products
66 K Field

*Including User Fee Funding


Factors Affecting Resource Distribution

- Historical
- Direct statutory mandates
- PDUFA dictates baseline level of effort in premarket review
- Advocacy: Orphan Drugs AIDS




Application Review: IND Process

- Current Performance Level
 - Process well managed and timely
 - First-time-in-human trial issues resolved
 - "Clinical holds" oversight



IND Process: Standards

- International Conference on Harmonization of Technical Requirements for Pharmaceuticals (ICH) Standards
 - Good Clinical Practices (GCP)
 - Toxicology protocols
 - Clinical Testing Guidance
- Indication - specific guidance not updated



Investigational New Drug Process: Issues

1. Performance: Extensive performance goals under "PDUFA II"
2. Access to Investigational Drugs
3. Status of Institutional Review Boards
4. Pediatric Drug Development
5. Research: Shorten drug development time & improve quality (CDDI)

New Drug Review: Performance

- **Timeliness: Meeting all PDUFA goals**
- **Openness: Over 50 Advisory Committee Meetings yearly**
- **Efficiency: Moving toward electronic submission**

New Drug Review: Standards

- **Requirements to study children, women, elderly, ethnic groups**
- **Antibiotic resistance**
- **Over-the-Counter Switches**
- **Chronically used drugs: patient follow-up**

New Drug Review: Issues

Standards

- **Drug Safety**
 - **Number of patients studied prior to marketing**
 - **Benefits to many Vs risks to few**
 - **Drug - drug Interactions**
- **Radio pharmaceuticals and PET drugs**

Application Review: Generic Drugs

- ⊛ **Current Performance Level**
 - Over 50% ANDA's reviewed in 180 days
 - Time to marketing has dropped from 40 months (1993) to 19 months (1997)
 - Additional streamlining occurring

Generic Drug Review: Issues

- ⊛ **Manufacturers calling for further shortening of review times**
- ⊛ **Congressional interest: Barriers to generic competition**
- ⊛ **Research: Non-oral dosage forms**

Application Review: Supplemental NDA's (New Uses)

- ⊛ **FDA "New Use Initiative"**
 - Guidance "Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products"
 - Guidance "FDA Approval of New Cancer Treatment Uses for Marketed Drug and Biological Products"

Product Quality Assurance: Performance

- ⊗ **Marketed drugs are of high quality**
- ⊗ **Efficiency gains: "SUPAC" Process**
- ⊗ **Not meeting every two year requirement for facility inspections**

Product Quality Assurance: Issues

- ⊗ **Maintaining adequate inspectional coverage in U.S.**
 - 3rd party audit?
 - 1st party audit?
- ⊗ **Inspection of foreign establishments**
 - Mutual recognition agreements

Product Quality Assurance: Issues (cont.)

- ⊗ **Manufacturing standards for bulk pharmaceuticals**
- ⊗ **Standards for Pharmacy Compounding**

Surveillance/Compliance

- **Health Fraud**
- **Dietary Supplements**
- **Marketed unapproved drugs**

Surveillance: Drug Marketing and Advertising: Issues

- **Direct-to-Consumer Advertising**
- **Disseminating of Reprints: FDAMA**
- **Consumer information on prescription drugs**
- **Pharmaceutical firm's role in managed care**

Surveillance: Human Subject Protection

- **Audits of clinical trials**
- **Audits of IRB's**
- **Training IRB's and clinical investigators**
- **International clinical trials**
- **Electronic data capture**

Safety of Marketed Drugs

⊗ **Premarket testing will not detect all problems/toxicity's**

- Rare events
- Events caused by use outside approved parameters
- Medication errors

Safety of Marketed Drugs (cont.)


⊗ **CDER is upgrading spontaneous reporting system (passive surveillance)**

⊗ **Active surveillance of various kinds has been suggested**

Communications


⊗ **Effective communication linked to drug safety**

- ⊗ **Prescription and OTC labeling**
- ⊗ **Drug development statistics**
- ⊗ **Communications research**



Summary

- **Drug regulatory system in U.S. is very effective and performing well**
- **Many expectations for improvement and competing priorities**
- **We need to hear from stakeholders**

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